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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,368	12/08/2000	Victor Rivera	394A US	1969

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EXAMINER	
PRIEBE, SCOTT DAVID	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,368	RIVERA ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *19-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14* is/are rejected.

7)☒ Claim(s) *13,15-18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/8/01, 8/5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the paper filed 2/5/04 is acknowledged. The traversal is on the ground(s) that restriction is not required but discretionary, many of the group share the same class and subclass and would pose no search burden, the restriction is incomplete; some of the groups overlap; claim 1 is generic to in vivo and ex vivo approaches. This is not found persuasive because restriction was required for the reasons set forth in the Office action of 10/1/03. While many of the groups share the same class and subclass, i.e. 424/93.2, this subclass is huge and encompasses a wide variety of different inventions, many of which are unrelated to each other. A search (3/10/04) of patents and published applications in 424/93.2 alone revealed 364 patents that made reference to an RSV promoter. A search of US patents is only part of the search that must be performed. A search of non-patent literature for references that include AAV and RSV promoters in their database records did not reveal the Lanuti et al. or Sterman et al. references provided by Applicant, which involved adenoviral vectors comprising an RSV promoter. This illustrates that a search of the elected invention would not necessarily identify prior art pertinent to non-elected inventions. Consequently, there would be a search burden. The restriction requirement was complete, claims 1-18 link inventions I-VI, as indicated at page 7 of the preceding Office action. Claims 1-18 are examined as they are directed to the elected invention or to the extent required to determine whether they are allowable. With respect to the possibility that some groups may overlap, i.e. include species in common, the claims are generic, and have been grouped according to common generic features,

e.g. using an AAV vector vs. an adenoviral vector, which are divergent in the art. With respect to claim 19, the issue of whether claim 19 properly depends from claim 1 is not relevant to whether in vivo gene delivery of a viral vector is independent or distinct from in vivo delivery of a recombinant cell.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed 2/5/04.

Information Disclosure Statement

The information disclosure statement filed 8/8/01 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but FR 2716460 A1 referred to therein as has not been considered. WO 95/22616 has been considered only with respect to the Abstract.

The information disclosure statement filed 8/5/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but JP 3028386 referred to therein has not been considered. The information disclosure statement filed 8/8/01 lists an abstract of JP 3028386, which was provided to the PTO. While this abstract has been considered, reference to it has been

crossed out on the PTO-1449 filed 8/8/01 because the citation is incomplete. The publication (or database) from which the abstract was obtained has not been identified in the citation. Should Applicant desire the abstract be cited on the face of a patent, a complete citation should be provided on a PTO-1449.

Drawings

New corrected drawings are required in this application because the text labeling in Figures 1 and 2 is illegible (type font is too small). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 1-18 are provisionally objected to because of the following informalities: the claims embrace non-elected inventions. Limiting the claims to introducing the transgene on an AAV vector would overcome this objection.

Claims 13 and 15-18 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependent claim (e.g. claims 6-12). See MPEP § 608.01(n). Accordingly, the claims 13 and 15-18 have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the limitation "the virus" in line 1. There is insufficient antecedent basis for this limitation in the claim, or in claims 1-5 from which it depends.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-6 and 14 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sterman et al. (Hum. Gene Ther. 9: 1083-1092, 1 May 1998).

Claims 7-12 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Sterman et al. (Hum. Gene Ther. 9: 1083-1092, 1 May

1998), as evidenced by the admission of prior art in the instant specification, GenBank Acc. No. U02455, and GenBank Acc. No. M77786.

Sterman discloses a method of "genetically engineering" human mesothelioma patients by introducing an adenoviral vector comprising a transgene. The transgene comprises an RSV promoter operably linked to coding sequence for HSV*tk*.

Sterman does not disclose the source or structure of the RSV promoter. However, as admitted in the specification at pages 1 and 11, the RSV promoter (a.k.a. RSV-LTR promoter) has been widely used for expression of transgenes in mammalian cells. The promoter was available from a variety of commercial sources. SEQ ID NO: 1 is disclosed as being a fragment obtained from one such commercially available mammalian expression vector, pREP8 (Invitrogen) that contains the RSV promoter (see also page 44). The specification discloses that rpDR2 (Clontech) also contains an RSV promoter. GenBank Acc. No. U02455 discloses the nucleotide sequence of rpDR2, of which nucleotides 148-671 are nearly identical to nucleotides 90-612 of instant SEQ ID NO: 1. The two sequences differ by four single nucleotide substitutions (nucleotides 237, 369, 496, and 524 of instant SEQ ID NO: 1) and a single nucleotide insertion in rpDR2 (after nucleotide 543 in SEQ ID NO: 1). Another well-known and commonly available mammalian expression vector, pRSVNeo, carries an RSV promoter sequence (GenBank Acc. No. M77786, complement of nucleotides 5-528) that is identical to that of rpDR2. Thus, the RSV promoters from various sources would have been expected to be interchangeable and structurally and functionally equivalent, and would also read on the limitations of claims 7-12, as shown by GenBank Acc Nos. M77786 and U02455. Consequently, even if the RSV promoter sequence used in the vector of Sterman did not include nucleotides 90-

612 (or the other recited subfragments) of SEQ ID NO: 1 specifically, it would have been obvious for one of ordinary skill in the art to have obtained it from pREP8 or any other commercially or widely available vector comprising an RSV promoter.

Claims 1-6 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Podsakoff et al., US 5,846,528.

Podsakoff teaches a method of systemic delivery of erythropoietin (EPO), such as human EPO, to a mammal, including humans, by *in vivo* intramuscular administration of an AAV vector carrying the coding sequence for the EPO under control of a promoter, e.g. see claims 2-13, 29-31. Podsakoff teaches that the RSV promoter is a suitable promoter, see col. 13, lines 11-12. Targets for the method include patients suffering from sickle cell disease and hereditary thalessemias (claim 4), which are well known human diseases (col. 1-2). See entire reference, particularly col. 8, lines 5-17; col. 11, line 33 to col. 13, line 16; col. 17-18, claims 2-13, 29-31. The examiner is unaware of non-human mammals suffering from sickle cell disease and hereditary thalessemias or public need or desire to treat such diseases in non-human mammals other than non-human mammals used as models of the human diseases.

Podsakoff does not disclose the structure of the RSV promoter to be used. However, claims 7-12 are either obvious or anticipated by Snyder for the same reasons as set forth in the rejection under 35 USC 102(b) over Sterman set forth above.

Claims 1-6 and 14 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Snyder et al., US 2002/0155580 (filed 27 May 1998).

Claims 7-12 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Snyder et al., US 2002/0155580, as evidenced by the admission of prior art in the instant specification, GenBank Acc. No. U02455, and GenBank Acc. No. M77786.

Snyder discloses a method of treating hemophilia A in a mammal by *in vivo* administration of an AAV vector comprising an RSV promoter operably linked to the coding sequence for human Factor VIII (hFVIII) to attain expression of hFVIII in . The primary target of the method are human hemophilia A patients. As noted in para. 0053-0054, the RSV promoter was chosen for its size and expression. See entire reference, particularly figure sheets 1, 2, 5-12, para. 0053, 0054, 0073-0077, 0080, 0090-0093, 0101-0128, claims 13 and 14.

Snyder does not disclose the structure of the RSV promoter used. However, claims 7-12 are either obvious or anticipated by Snyder for the same reasons as set forth in the rejection under 35 USC 102(b) over Sterman set forth above.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Woo et al., WO 95/05835, discloses delivery of an adenoviral vector comprising an RSV promoter operably linked to coding sequence for HSV *tk* to baboons (pages 36-41).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

Scott D. Priebe
Primary Examiner
Art Unit 1632